

CASE REPORT

Concurrent, successful management of bipolar I disorder with comorbid alcohol dependence via aripiprazole long-acting injection: A case report

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Abstract

Alcohol dependence is frequently comorbid with bipolar I disorder. Aripiprazole and its long-acting injection have demonstrated efficacy in the treatment and prevention of bipolar I disorder and its attendant symptoms, especially manic episodes. However, whether aripiprazole can alleviate alcohol dependence remains controversial. We report the case of a 47-year-old woman who had been diagnosed with bipolar I disorder and alcohol dependence, characterized by poor adherence to pharmacological treatment and our hospital's alcoholic treatment program. Consequently, she was repeatedly hospitalized several times per year due to manic episodes and heavy drinking. After treatment with aripiprazole long-acting injection at a dosage of 400 mg/mo intramuscularly, she has been relapse-free for over 2 years. Aripiprazole long-acting injection might therefore be effective for treating patients with bipolar disorder and a comorbid diagnosis of alcohol dependence.

KEYWORDS

alcohol dependence, alcohol use disorder, bipolar I disorder, dopamine, long-acting injectable aripiprazole

1 | INTRODUCTION

Patients with bipolar I disorder frequently have alcohol dependence as a comorbid psychiatric disease (23%-38%)¹⁻³. Various evidence-based pharmacological options are available for the treatment of bipolar I disorder⁴, among which aripiprazole and its long-acting injection (ALAI) are reportedly efficacious for preventing manic episodes^{5,6}. However, only a few drugs are available for the treatment of alcoholism, including acamprosate, naltrexone, and disulfiram; whether aripiprazole can treat alcohol dependence remains controversial^{7,8}.

While nearly all patients with bipolar I disorder require long-term medication to prevent relapse and recurrence, adherence to pharmacological treatment among patients with bipolar disorder is

reportedly low⁹; limited adherence to medical treatment also characterizes patients with alcohol dependence¹⁰. Resolving poor adherence to medical treatment in patients with bipolar disorder or alcohol dependence thus warrants investigation.

Here, we describe a patient diagnosed with bipolar I disorder and alcohol dependence who maintained sobriety for over 2 years without recurrences of any mood episodes following administration of ALAI.

2 | CASE

A 47-year-old woman had recurrent depressive episodes with appetite loss, self-harm behavior, suicidal ideation, and anxiety symptoms,

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including panic attacks, from her late teens. At the age of 35 years, she first visited a psychiatric clinic and was diagnosed with major depressive disorder; she began taking paroxetine but continued to experience recurrent depressive episodes. Moreover, she began to engage in heavy alcohol consumption at approximately 39 years of age. She was referred to our hospital at the age of 40 years. Despite attempts to treat her alcoholism with acamprosate (1998 mg/day) and our hospital's alcoholism treatment program, she was hospitalized three times due to alcohol withdrawal delirium. Deterioration of her liver function was evinced by the following laboratory findings when she engaged in the heaviest alcohol consumption: serum aspartate transaminase glutamate oxaloacetate transaminase, 549 IU/L; alanine transaminase glutamic pyruvic transaminase, 132 IU/L; and gamma-glutamyl transpeptidase, 794 IU/L.

At the age of 43 years, her behavior evinced a first manic episode: feelings of grandiosity, increased talkativeness, and grandiose delusions. We therefore diagnosed her with bipolar I disorder comorbid with alcohol dependence. Regarding pharmacotherapy for her bipolar I disorder, we sought to manage the depressive and/or manic symptoms with the following atypical oral antipsychotic monotherapies: quetiapine, 500 mg/d; olanzapine, 10 mg/d, and combination therapies of antipsychotics plus mood stabilizers: valproate, 1000 mg/d; and carbamazepine 400 mg/d when she was in hospital. Although these pharmacotherapies allowed temporary remission, which satisfied the section of bipolar and related disorders in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), of her bipolar symptoms, such that she could be discharged, her adherence to medical treatments did not improve; they did not improve her adherence to medical treatments. After the patient had been diagnosed with bipolar I disorder, she was hospitalized an additional four times due to depressive or manic episodes with psychosis because of poor adherence to the prescribed regimen. We did not prescribe lithium because of her history of hypothyroidism, for which she was undergoing treatment during the same period.

When the patient was hospitalized for the eighth time due to manic episodes accompanied by heavy drinking at the age of 44 years, we attempted to treat her with ALAI, followed by pharmacotherapy with oral aripiprazole tablets at a maximum daily dosage of 30 mg/d. After explaining to the patient and her family that ALAI was an off-label therapy for bipolar disorder in Japan, we obtained consent from both to perform ALAI treatment. We first began prescription of ALAI at a dose of 400 mg/mo intramuscularly (ALAI 400), in combination with acamprosate, 1998 mg/d. Neither drug-induced any adverse events in the patient. Three months after commencing ALAI treatment, the patient was discharged from our hospital due to remission of her bipolar symptoms. She regularly returned to the outpatient department of our hospital for follow-up visits. Over the following 2 years, she maintained sobriety, did not crave alcohol, and did not have any recurrent mood episodes. In addition, her thyroid function was well controlled before and after ALAI treatment. After her last discharge, she obtained a teacher qualification and has been employed as a full-time worker.

3 | DISCUSSION

We herein report the case of a 47-year-old woman with bipolar I disorder and alcohol dependence characterized by resistance to pharmacotherapy for bipolar disorder, as well as resistance to our hospital's alcoholism treatment program and acamprosate for alcohol dependence. To the best of our knowledge, this is the first report to demonstrate the successful concurrent management of bipolar I disorder and alcohol dependence with ALAI 400.

Accumulating evidence suggests that dysregulation in the mesolimbic dopamine system is involved in the pathophysiology of alcoholism¹¹⁻¹³. Previous animal and human studies have reported that aripiprazole, which acts as a partial agonist of dopamine D2 receptors, can potentially treat alcohol dependence¹⁴⁻¹⁶. However, two randomized clinical trials have found conflicting results regarding the efficacy of aripiprazole in addressing alcohol dependence^{7,8}.

The first randomized placebo-controlled study with a sample of 295 participants found that an aripiprazole regimen, in which the drug was initiated at 2 mg/d and titrated to 30 mg/d over the course of 28 days, failed to achieve a significant percentage of abstinent days among patients with alcohol dependence in a 12-week period⁷; the authors of that study proposed that the high incidence of drop-out patients, aripiprazole group (40.3%) vs placebo group (26.7%), who were treated with a daily aripiprazole dosage of more than 15 mg influenced the primary outcome of their study⁷. The second double-blind trial that compared the efficacy of a flexible dosage of aripiprazole (5-15 mg/d) to that of a fixed dosage of naltrexone (50 mg/d) in treating alcohol dependence showed that aripiprazole and naltrexone similarly affected remaining abstinence and craving for alcohol⁸. In addition, a placebo-controlled study found that oral aripiprazole treatment administered at a maximum dosage of 15 mg/d reduced drinking in alcoholic patients with low impulse control more effectively than in those without low impulse control¹⁷.

Considering the aforementioned evidence of the capacity ALAI to prevent relapse in patients with bipolar I disorder, moderate dosages of aripiprazole treatment may help to improve maintenance treatment of bipolar disorder and the management of alcohol abstinence, as was observed in the present case; however, the precise equivalent dose of oral aripiprazole tablets administered daily that will achieve the same effect as ALAI 400 is unclear.

In addition, switching from oral antipsychotics to LAI antipsychotics is reportedly effective in promoting adherence among patients with psychotic disorders¹⁸. Thus, in pharmacological treatments of bipolar disorders and alcohol dependence, LAI treatment may improve relapse prevention in patients with poor adherence to pharmacotherapy.

4 | CONCLUSION

Considering that bipolar disorders are frequently comorbid with alcohol dependence, our findings in this case indicated that ALAI may



be an efficacious option for the treatment of patients with bipolar disorder and alcohol dependence who respond well to oral aripiprazole and experience repeated relapse due to poor adherence to medical treatment. Further clinical trials are needed to validate our findings.

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CONFLICT OF INTEREST

T.K. has received honoraria as a speaker/consultant from Dainippon Sumitomo, Otsuka, Nihon Shinyaku, and Yoshitomiya. T.H. has received personal fees from research support of a clinical trial managed by a global bracket company. H.S. has received honoraria as a speaker from Daiichi-Sankyo and Janssen.

AUTHOR CONTRIBUTIONS

T.K. was the consulting psychiatrist for the patient. T.H. and H.S. supervised T.K. in the treatment of the patient. All authors contributed to the writing and revision of the manuscript, and all authors have read and approved the submitted version of the manuscript.

INFORMED CONSENT

The patient provided written informed consent for the publication of this case report. The treatment in this case report was performed in accordance with the World Medical Association's Declaration of Helsinki.

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